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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **TOLUIDINE BLUE O DRUG SUBSTANCE AND USE THEREOF FOR IN VIVO STAINING AND CHEMOTHERAPEUTIC TREATMENT OF DYSPLASTIC TISSUES**

(57) Abstract: The invention comprises an improved process for preparing TBO drug products includes the steps: (1) synthesising an indamine; (2) converting said indamine into an S-indaminyll thiosulfate; and (3) adding an oxidizing catalyst agent, complexing agent, and an acid to said S-indaminyll thiosulfate to formulate TBO and C-4-methyl regioisomer, and derivatives thereof. The invention further comprises new compositions of matter that are useful for detecting dysplastic tissue, as well as, treating dysplastic tissue, namely, TBO products predominantly comprised of peaks eight, peak six, or a combination thereof. *N,N*-dimethyl-*p*-phenylenediamine as a starting material results in a TBO product composition comprised of peaks eight, seven, six, and five in the approximate ratios 33:5:5:1, respectively. Whereas *N*-dimethyl-*p*-phenylenediamine as a starting material results in a TBO demetylated product composition comprised of peaks six, five, tree and two in the approximate ratio 33:5:5:1, respectively. The invention further comprises an improved PLC method for analyzing the improved TBO drug product, the improvement comprising the addition of an ion-pairing reagent in a first mobile phase and forming a second mobile phase composition comprising 50% alcohol by volume.

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/17720

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 49/00  
US CL : 424/9.7

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/1.11, 9.1, 9.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
biosis, medline, uspatfull, embase, caplus, registry file

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,086,852 A (BURKETT) 11 July 2000 (11.07.2000), see entire document, especially, columns 17-22, claims 1-10.	1-23
A	US 6,194,573 B1 (BURKETT) 27 February 2001 (27.02.2001), see entire document, especially, column 10, claim 1.	1-23
A	US 6,372,904 B2 (BURKETT) 16 April 2002 (16.04.2002), see entire document, especially, columns 10-12, claims 1-5.	1-23

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

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- "P" document published prior to the international filing date but later than the priority date claimed

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- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

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